Bicarbonate haemodialysis as a treatment of metformin overdose

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Introduction

Metformin is a biguanide oral hypoglycaemic agent commonly used in the treatment of diabetes mellitus. Metformin is excreted largely by the kidneys and binds only negligibly to plasma proteins. Toxicity is usually seen when metformin is prescribed to patients with renal insufficiency, and it can produce a severe lactic acidosis. Other factors that increase blood lactate concentrations are usually present, for example hypoxia, liver disease, or alcohol abuse. In these cases the plasma concentration of metformin is not necessarily abnormally high [1].

A healthy young man took a large dose of metformin together with a smaller dose of nabumetone and glibenclamide in a deliberate attempt to harm himself. The overdose was associated with a profound lactic acidosis and he was successfully treated by haemodialysis with bicarbonate buffer.

Case report

A 29-year-old man was admitted to a general medical ward 2 h after taking a deliberate overdose of his father's metformin, glibenclamide, and nabumetone. The exact quantity of tablets taken was not known but it is thought the quantity of glibenclamide and nabumetone taken was small. The patient had been previously well and had no past medical history of diabetes or renal impairment. He did not take any other prescribed or illicit drugs.

On admission his Glasgow Coma Scale was 10/15. Pulse rate was 102 regular and systolic blood pressure was 150 mmHg. Respiration rate was 20 per minute. Initial investigations revealed hypoglycaemia (glucose 0.6 mmol/l). Serum sodium was 148 mmol/l, potassium 4.5 mmol/l, bicarbonate 17 mmol/l, urea 3.4 mmol/l and creatinine 167 µmol/l. Blood alcohol was 36 mmol/l. ECG and CXR were normal.

Initial treatment included 100 ml 50% glucose i.v., oxygen at 10 l/min and when his conscious level improved, a gastric lavage. His conscious level returned to 15/15 on the GCS. Blood glucose was measured at 18 mmol/l.

Over the next 3 h the patient began to complain of nausea and abdominal pain and was noted to become increasingly agitated and tachypnoeic. Pulse rate was 190/min and multifocal ectopic beats were demonstrated on ECG. Systolic blood pressure was 110 mmHg. Serum electrolytes and arterial blood gases were rechecked and a serum lactate was measured. Hydrogen ion concentration was 110 nmol/l, bicarbonate 2 mmol/l, \( \text{PaCO}_2 \) 1.7 kPa, \( \text{PaO}_2 \) 19.2 kPa, and serum lactate 31 mmol/l.

He was transferred to the renal unit where he was haemodialysed for 10 h using a sodium bicarbonate buffer. This treatment was associated with an improvement in his clinical condition. Hydrogen ion concentration and bicarbonate levels returned to normal and his serum lactate fell to 3.7 mmol/l after 24 h. (Table 1). There was a transient deterioration in his serum urea and creatinine to a maximum of 11.8 mmol/l and 398 µmol/l on day 3. By day 10 these had resolved to 8.0 and 118 mmol/l respectively. Liver function and clotting studies remained within normal reference range.

The patient was discharged on the 7th day after admission and was followed up on an out-patient basis, where no further complications have been noted.

Discussion

Deliberate self-poisoning with oral hypoglycemic agents is rare. The lactic acidosis associated with metformin toxicity is described in the medical literature

| Table 1. |
|-------------------|--------------------|--------------------|
| Hours after start of HD | Lactate conc. (mmol/l) | Serum bicarbonate (mmol/l) |
| 0                  | 31.0               | 2                  |
| 2                  | 24.4               | 7                  |
| 7                  | 7.7                | 21                 |
| 9                  | 4.7                | 28                 |
in the context of diabetes and or other major illnesses [2].

In our case an otherwise healthy patient was admitted as a result of a deliberate overdose of tablets that included metformin. He soon developed a profound lactic acidosis without evidence of tissue hypoxia (Type B2 in Cohen and Woods’ classification [3]). The relationship between lactic acidosis and mortality in the absence of tissue hypoxia is unknown but in intensive care patients mortality rates have been demonstrated to be as high as 80% [4].

The treatment of lactic acidosis is therefore important, but no consensus exists as to therapy. The use of sodium bicarbonate is well known but controversial. Recent reviews highlight that there has been no rigorous testing of the efficacy of bicarbonate of supportive therapy in the clinical setting [4,5]. There are theoretical disadvantages of using intravenous bicarbonate including (1) leftward shift of the oxyhaemoglobin dissociation curve, (2) excess sodium load, (3) rebound metabolic alkalosis, (4) disturbances in serum potassium and calcium, and (5) reflex vasodilatation after bolus injection. Furthermore, bicarbonate is a carbon-dioxide-producing buffer and it is postulated that the production of carbon dioxide might decrease myocardial contractility [6]. The use of alkali in cardiopulmonary arrest is no longer recommended [7].

However, in the absence of underlying cardiovascular, respiratory, or renal pathology the use of bicarbonate dialysate resulted in a satisfactory outcome in our patient.

Haemodialysis with bicarbonate dialysate allows clearance of metformin [8] and allows bicarbonate to be administered without the associated risks of intravenous administration.

In conclusion, metformin overdose even in otherwise healthy patients may produce a profound and life-threatening lactic acidosis. There have been no clinical trials comparing therapeutic modalities in this situation. We suggest that haemodialysis with bicarbonate as the buffer is an effective treatment in this situation.

References


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